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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,609	12/17/2001	Richard L. Vandlen	P0712C5	5365

9157 7590 08/08/2003

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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/022,609	Vandlen et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 27, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *20* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7 & 12
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Sequence Rules

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because 37 CFR 1.821 (a)(2)(c-d) states that *each sequence disclosed must appear separately in the* "Sequence listing" and *in the text of the description* and claims whenever described. For example, the appropriate SEQ ID NOs must be recited on pages 14 (lines 1, 5, 11, 13, 15, 16, 18 & 19), 15 (line 23), 16 (lines 5, 6 & 26), 19 (lines 6 & 10), 32 (line 13), 36 (line 6) & 84 (lines 10 & 31). See MPEP 2422 & 2431.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Note that failure to respond to both the requirements for sequence compliance and the Office action below will be held as nonresponsive, and may result in abandonment of this application.

Election/Restriction

2. Applicant's election of Group III (claim 20) in Paper No. 7, and cancellation of all other pending claims, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 20 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 & 15-25 of U.S. Patent No. 5,859,206. Although the conflicting claims are not identical, they are not patentably distinct from each other because all these claims within '206 claim antibodies that bind heregulin 2-α, as also claimed in the instant application. In other words, claim 20 of the instant application is generic to these claims within '206, in which the species claims of '206 anticipate the generic claim of the instant application.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Page 10 describes the heregulin 2-α protein of SEQ ID NO:11. Page 14 states that "the biologically active and antigenically active HRG2-α polypeptides that are the subject of this invention include... other animal species of HRG2-α polypeptides such as rabbit, rat, porcine, non-human primate, equine, murine, and ovine HRG2-α and alleles or other naturally occurring variants of the forgoing and human sequences". In contrast, only the human HRG2-α polypeptide sequence of SEQ ID NO:11 is described. No other species of heregulin 2-α polypeptide is described. Likewise, no allelic variants of the human heregulin 2-α of SEQ ID NO:11 are described. Therefore, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of antigenic polypeptides from different species, or allelic variants thereof, which would generate functional antibodies to such, because it is unknown and not described what structurally constitutes such generic antigenic HRG2-α polypeptides from different species, or allelic variants thereof. Thus, the written description requirements under 35 U.S.C. 112, first paragraph are not met.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999. See especially Examples 11, 12 & 17.

5. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for various types of antibodies directed against specific epitopes within the heregulin 2-α protein molecule of SEQ ID NO: 11, does not reasonably provide enablement for antibodies directed against structurally and functionally uncharacterized proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification describes the human heregulin 2- polypeptide of SEQ ID NO: 11. However, the name, "heregulin 2-" polypeptides (i.e., as defined on pages 12-14 of the specification) encompass any biologically functional equivalent protein, as well as "variants and derivatives", and any random "fragments", "substitutions", "extensions, deletions, or insertions", which sets forth little structural and functional characteristics. In contrast, no functional epitope fragments nor functional epitopes from any such polypeptide are disclosed within the specification. In fact, the specification fails to teach what amino acid residues constitute a single functional heregulin 2-α-specific epitope, or what epitopes distinguish a heregulin 2-α-specific epitope from any different heregulin 2-α-related protein molecule that possesses none of the desired functions of the instant invention. In other words, generation of any such antibodies without further recited and definable structural and assayable functional characteristics would be expected by the skilled artisan to result in antibodies that no longer bind to the heregulin 2-α polypeptide of SEQ ID NO: 11, or alternatively cross-react with different proteins. For example,

Geysen et al. teach that random amino acid changes to a tetrameric peptide/epitope, which includes conservative substitutions to the same antigen, have "frequently been associated with loss of antibody binding" (e.g., pg. 38, 1st col., 2nd *pp*). Thus, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any specific heregulin 2-α antibody binding reaction would prevent the skilled artisan from determining whether any random modification or truncation to the human heregulin 2-α protein sequence depicted as SEQ ID NO: 11 could be made that successfully generate the desired antibodies of the instant invention, because any random modification/ truncation manifested within a heregulin 2-α protein itself would be predicted to adversely alter its biologically active 3-dimensional conformation, and therefore, the antigenic/binding site itself, without requiring undue experimentation to determine otherwise.

Information Disclosure Statement

6. The information disclosure statement filed 12/17/01 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered, for those references crossed out.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements

based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 C(1).

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
August 4, 2003